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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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(54) Title: ADENO-ASSOCIATED VIRUS PRODUCER SYSTEM

(57) Abstract: The present invention provides the use of a replication competent herpes virus which (a) lacks a functional wild-type HSV ICP27 gene; and (b) comprises an ICP27 gene encoding an ICP27 protein which allows replication of said herpes virus to occur and which has a reduced ability to inhibit RNA splicing compared to wild-type HSV ICP27 in the production of an adeno-associated virus (AAV) vector.

INTERNATIONAL SEARCH REPORT

PCT/GB 03/01585

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/86

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SOLIMAN TARIK M ET AL: "Shuttling of the herpes simplex virus type 1 regulatory protein ICP27 between the nucleus and cytoplasm mediates the expression of late proteins." JOURNAL OF VIROLOGY, vol. 71, no. 12, December 1997 (1997-12), pages 9188-9197, XP002247080 ISSN: 0022-538X page 9195 figure 1	1-27

-/—

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 July 2003.	24/07/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Guarinos Viñals, E

INTERNATIONAL SEARCH REPORT

PCT/GB 03/01585

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CONWAY ET AL: "Recombinant adeno-associated virus type 2 replication and packaging is entirely supported by herpes simplex virus type 1 amplicon expressing rep and cap" JOURNAL OF VIROLOGY, THE AMERICAN SOCIETY FOR MICROBIOLOGY, US, vol. 71, no. 11, November 1997 (1997-11), pages 8780-8789, XP002102271 ISSN: 0022-538X page 8785, right-hand column page 8788, left-hand column	1-27
A	COFFIN R S ET AL: "Gene delivery to the central and peripheral nervous systems of mice using HSV1 ICP34.5 deletion mutant vectors" GENE THERAPY, MACMILLAN PRESS LTD., BASINGSTOKE, GB, vol. 3, no. 10, October 1996 (1996-10), pages 886-891, XP002108600 ISSN: 0969-7128 figure 1	10,16
A	ZHANG X ET AL: "HIGH-TITER RECOMBINANT ADENO-ASSOCIATED VIRUS PRODUCTION FROM REPLICATING AMPLICONS AND HERPES VECTORS DELETED FOR GLYCOPROTEIN H" HUMAN GENE THERAPY, XX, XX, vol. 10, no. 15, 10 October 1999 (1999-10-10), pages 2527-2537, XP000906820 ISSN: 1043-0342 figure 1	9

INTERNATIONAL SEARCH REPORT

PCT/GB 03/01585

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 26 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: 1-27 partially
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/GB 03 /01585

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-27 partially

Present claims 1-27 relate to a ICP27 protein defined by reference to a desirable characteristic or property, namely its capacity to allow herpes virus replication and its reduced ability to inhibit RNA splicing compared to wild type ICP27.

The claims cover all ICP27 proteins having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such proteins. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the protein by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the ICP27 proteins comprising the double substitutions specified in page 9, lines 9-20 of the description: R480H + S334L; R480H + V487I; R480H + V496I

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

SEQUENCE LISTING

<110> UNIVERSITY COLLEGE LONDON

<120> ADENO-ASSOCIATED VIRUS PRODUCER SYSTEM

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<150> GB 0208390.5
<151> 2002-04-11

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35 40 45

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